REMARKS

Claims 15-26 have been rejected and are currently pending. In light of the following remarks, Applicants respectfully request reconsideration and allowance of claims 15-26.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 15-26 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Specifically, the Examiner concluded that a skilled artisan would have had to resort to undue experimentation to practice the full scope of the claimed invention.

Applicants respectfully disagree. The enablement requirement consists of two prongs: (1) the specification must adequately describe how to make the invention; and, (2) the application must describe how to use the invention. *See*, 35 U.S.C. § 112, first paragraph. A considerable amount of experimentation is permissible to make and use the claimed invention, particularly if it is routine experimentation. *See, e.g., PPG Indus., Inc. v. Guardian Indus. Corp.,* 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The amount of experimentation that is permissible depends upon a number of factors. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). These include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. *Id.* When making a determination of enablement, the Examiner must consider all evidence related to the *Wands* factors, and not focus on a single factor, while ignoring one or more of the others. M.P.E.P. § 2164.01(a) citing *In re Wands*, 858 F.2d at 737.

Applicants respectfully submit that the originally filed specification fully enables the claimed invention. In particular, the numerous working examples provided within Applicants' specification demonstrate that a person of ordinary skill in the art could have made and used the claimed invention to engender a biological response in a mammal. For instance, the working examples demonstrate that a PNA oligomer having a sequence that targets the non-coding strand

the mu-1 receptor (designated the MU1R-PNA oligomer) engenders sequence specific biological response after *in vivo* administration. *See*, *e.g.*, Example 2. Specifically, intraperitoneal administration of the MU1R-PNA oligomer to a mammal engendered a sequence specific biological response characterized by a lack of morphine responsiveness as determined by the tail flick anti-nociceptive response. In addition, the working examples demonstrate that a PNA oligomer having a sequence that targets the coding strand of neurotensin receptor-1 nucleic acid (designated the sense-NTR1-PNA oligomer) engenders a sequence specific biological response after *in vivo* administration. *See*, *e.g.*, Example 8. Specifically, intra-peritoneal administrations of the sense-NTR1-PNA oligomer to a mammal engendered a sequence specific biological response characterized by a reduction in neurotensin responsiveness.

The working examples provided in Applicants' specification also demonstrate that a PNA oligomer having a sequence that targets the non-coding strand of neurotensin receptor-1 nucleic acid gene but contains mismatches (designated the mismatch-NTR1-PNA oligomer) engenders a sequence specific biological response after *in vivo* administration. *See*, *e.g.*, Example 8. Specifically, intraperitoneal administration of the mismatch-NTR1-PNA oligomer to a mammal engendered a sequence specific biological response characterized by a reduction in neurotensin responsiveness that was altered with respect to the responses engendered by the NTR1-PNA oligomer that does not contain the mismatches. Moreover, the working examples demonstrate that oral administration of the NTR1-PNA oligomer engenders a sequence specific biological response. *See*, *e.g.*, Example 4. Specifically, oral administration of the NTR1-PNA oligomer engendered a sequence specific biological response characterized by a reduction in neurotensin responsiveness as well as a reduction in neurotensin receptors both in brain and the periphery. Thus, the working examples within Applicants' specification demonstrate that one skilled in the art could have followed the teachings of the originally filed specification to use PNA oligomers as claimed without undue experimentation. Hence, claims 15-26 comply with the enablement requirement.

It is important to note that, in every working example referenced above, the targeted PNA oligomer was the first PNA oligomer that Applicants administered to a mammal. *See*, *e.g.*,

Declaration by Dr. Elliott Richelson from U.S. Pat. App. Ser. No. 09/016,685. Accordingly, the evidence shows that Applicants readily designed and administered sense, anti-sense, and mismatch PNA oligomers that were successful in engendering biological responses in mammals. For example, the MU1R-PNA oligomer was the first PNA oligomer targeting the non-coding strand of the mu-1 receptor that Applicants administered to a mammal. *Id.* at paragraph 6. In addition, the mismatch-NTR1-PNA oligomer was the first PNA oligomer targeting the non-coding strand of the neurotensin-1 receptor and containing a mismatch that Applicants administered to a mammal. *Id.* at paragraph 5. Moreover, the sense-NTR1-PNA oligomer was the first PNA oligomer targeting the coding strand of the neurotensin-1 receptor that Applicants administered to a mammal. *Id.* at paragraph 8. Thus, the Declaration of Dr. Elliott Richelson provides additional evidence demonstrating that one skilled in the art could have followed the teachings of the originally filed specification to use PNA oligomers as claimed without undue experimentation.

The Examiner noted that the background section of the above referenced application suggested that there were problems associated with cellular uptake of PNA oligomers. The mere recitation of issues with PNAs that were unresolved before Applicants' effective filing date does not demonstrate that Applicants' specification does not enable the presently claimed methods. Applicants' specification provides numerous working examples demonstrating cellular uptake of various PNA oligomers. In addition, Applicants' specification describes *in vitro* assays to screen PNA molecules (*e.g.*, Applicants' specification at page 17). Thus, the guidance and direction provided within Applicants' specification fully enables the claimed invention.

Moreover, the Examiner interpretation of the claims is not consistent with the Federal Circuit's instructions that claims be read "in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364 (Fed. Cir. 2004); *See also*, *e.g.*, *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005), and *In re Cortright*, 165 F.3d 1353, 1359, (Fed. Cir. 1999). In particular, the Examiner has misconstrued the term "treating" in the preamble of claim 15 as being equivalent to "treating a disease." Applicants' specification discloses that a sequence specific biological response is any

response in a living cell that is attributed to the actual sequence of PNA oligomer, such as the modulation of protein expression. Thus, a person of ordinary skill in the art would interpret the claimed methods for treating cells as a method of subjecting cells to a chemical reagent so as to engender a biological response. This interpretation is also consistent with the definition of "treat" in *Webster's Third New International Dictionary Unabridged* (1993), a copy of which is provided with the enclosed PTO-1449 form. The Examiner, however, has focused on a few lines of the specification to the exclusion of the teachings of the specification as a whole, and how the specification as a whole would be interpreted by one of ordinary skill in the art.

Contrary to the Examiner's assertion, an interpretation of the claim language that is consistent with Applicants' specification demonstrates that the pending claims are not overly drawn. For example, the claims do not encompass *any* polyamide nucleic acid, nor do the claims suggest that the PNA oligomers are effective to treat *any and all* disease conditions in a mammal. Instead, the claimed methods of treating cells present in a mammal involve administering a PNA oligomer to cells such that the PNA oligomer engenders a biological response in a sequence specific manner. The backbone linkages of the polyamide nucleic acid oligomer are neutral amide backbone linkages, and the PNA oligomer contains a sequence that is complementary to a target nucleic acid present in the mammal. The biological response is associated with the target nucleic acid, and the administration is an extracranial administration. Thus, as explained above, Applicants' specification fully enables the full breadth of the claimed invention.

For these reasons and others, Applicants respectfully request withdrawal of the rejection of claims 15-26 under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 15-25 under 35 U.S.C. § 102(e) as allegedly being anticipated by the Buchardt *et al.* reference (U.S. Pat. Pub. No. US2002/0146718).

Applicants respectfully disagree. The present claims recite a method involving administering a PNA oligomer to cells present in a mammal under conditions wherein the PNA

oligomer engenders a biological response in a sequence specific manner. At no point does the Buchardt *et al*. reference disclose the successful *in vivo* administration of a PNA oligomer to engender a biological response in a sequence specific manner. Thus, the cited reference does not anticipate Applicants' claimed invention.

For at least these reasons, Applicants respectfully request withdrawal of the rejection of claims 15-25 under 35 U.S.C. § 102(e).

CONCLUSION

Applicants assert that claims 15-26 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone the undersigned attorney if such contact would advance prosecution of this Application. Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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